

532,297
10/532297

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
6 May 2004 (06.05.2004)

PCT

(10) International Publication Number
WO 2004/037261 A1

(51) International Patent Classification⁷: **A61K 31/506**,
45/06, A61P 9/12

Alexander [US/US]; 1127 Philip Street, New Orleans, LA
70130 (US).

(21) International Application Number:
PCT/IB2003/004671

(74) Agents: **HOXIE**, Thomas et al.; Novartis AG, Corporate
Intellectual Property, CH-4002 Basel (CH).

(22) International Filing Date: 20 October 2003 (20.10.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SE, SG, SK, SY, TJ,
TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/421,318 25 October 2002 (25.10.2002) US

(84) Designated States (*regional*): Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR).

(71) Applicant (*for all designated States except US*): **THE
ADMINISTRATORS OF THE TULANE EDUCA-
TIONAL FUND** [US/US]; 1430 Tulane Avenue, SL-13,
New Orleans, LA 70112 (US).

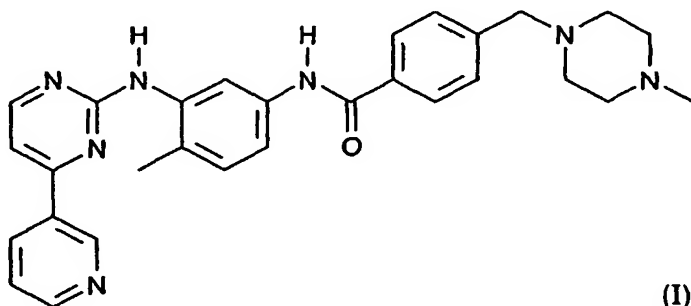
Published:
— with international search report

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): **LASKY, Joseph**,

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: USE OF N-'5-'4-(4-METHYLPIPERAZIOMETHYL)-BENZOYLAMIDO!-2-METHYLPHENYL!-4-(3-PYRIDYL)2-PYRIDINE-AMINE FOR THE TREATMENT OF PULMONARY HYPERTENSION



(57) Abstract: The present invention pertains to the use of 4-(4-methylpiperazin-1-yl-methyl)-N[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino]phenyl]-benzamide of the formula I or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of pulmonary hypertension.

(I)

WO 2004/037261 A1

INTERNATIONAL SEARCH REPORT

PCT/03/04671

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/506 A61K45/06 A61P9/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data, WPI Data, PAJ, PASCAL, SCISEARCH, CANCERLIT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 03 077892 A (UNIV MELBOURNE ; GILBERT RICHARD ERNEST (AU); KELLY DARREN JAMES (A) 25 September 2003 (2003-09-25) page 3, line 23 - page 4, line 10 page 9, paragraph 4 page 12, paragraph 3 page 14, paragraph 3 - page 15, paragraph 2 page 18, paragraph 5 page 19, paragraph 4 page 20, paragraph 2 page 24, paragraph 3 page 24, paragraph 5 - page 25, paragraph 2 page 26, paragraph 2	1, 3, 6-10
X	WO 02 43746 A (MONDOBIOTECH SA ; BLOCK LUTZ HENNING (DE)) 6 June 2002 (2002-06-06) page 1, line 15 - line 16 page 12, line 27 - page 13, line 6 -/-	1, 2, 5-7, 10

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

15 January 2004

Date of mailing of the international search report

16/02/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Albrecht, S

INTERNATIONAL SEARCH REPORT

PCT/03/04671

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 99 03854 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); BUERGER HANS MICHA) 28 January 1999 (1999-01-28) cited in the application page 3, paragraph 4 page 9, paragraph 4 -page 10, paragraph 2 page 11, paragraph 1 ---	1-10
Y	DATABASE MEDLINE 'Online! US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; December 1997 (1997-12) HUANG Q ET AL: "'Changes of PDGF-alpha and beta receptor gene expression in hypoxic rat pulmonary vessels!" Database accession no. NLM10453542 XP002266955 abstract & ZHONGGUO YI XUE KE XUE YUAN XUE BAO. ACTA ACADEMIAE MEDICINAE SINICAE. CHINA DEC 1997, vol. 19, no. 6, December 1997 (1997-12), pages 470-473, ISSN: 1000-503X ---	1-10
Y	TANABE YOSHIYUKI ET AL: "Increased expression of PDGF receptor beta gene in MCT-induced pulmonary hypertensive rats" JAPANESE JOURNAL OF PHARMACOLOGY, vol. 79, no. SUPPL. 1, 1999, page 72P XP009023742 72nd Annual Meeting of the Japanese Pharmacological Society;Sapporo, Japan; March 22-25, 1999 ISSN: 0021-5198 the whole document ---	1-10
Y	JUNBAO D ET AL: "Impact of nitric oxide on platelet-derived growth factor expression in intrapulmonary arteries of rats with hypoxic pulmonary vascular structural remodeling" CARDIOVASCULAR ENGINEERING 2001 GERMANY, vol. 6, no. 1, 2001, pages 62-67, XP009023789 ISSN: 1432-9077 pages 62-63, chapter "Introduction" pages 65-66, chapter "PDGF Expression" page 66, chapter "Linear Correlation Analysis" page 66, column 2, paragraph 3 -----	1-10

INTERNATIONAL SEARCH REPORT

CT/IB 03/04671

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 10 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/03/04671

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 03077892	A	25-09-2003	WO	03077892 A2	25-09-2003
WO 0243746	A	06-06-2002	AU	2072002 A	11-06-2002
			CA	2428552 A1	06-06-2002
			WO	0243746 A2	06-06-2002
			EP	1337557 A2	27-08-2003
WO 9903854	A	28-01-1999	AT	251152 T	15-10-2003
			AU	740713 B2	15-11-2001
			AU	8975998 A	10-02-1999
			BR	9810920 A	15-08-2000
			CN	1264375 T	23-08-2000
			DE	69818674 D1	06-11-2003
			WO	9903854 A1	28-01-1999
			EP	0998473 A1	10-05-2000
			HU	0003230 A2	28-06-2001
			ID	24093 A	06-07-2000
			JP	3276359 B2	22-04-2002
			JP	2001510192 T	31-07-2001
			NO	20000227 A	17-01-2000
			NZ	502295 A	21-12-2001
			PL	338129 A1	25-09-2000
			RU	2208012 C2	10-07-2003
			SK	432000 A3	12-06-2000
			TR	200000060 T2	21-09-2000
			TW	491845 B	21-06-2002
			US	2002115858 A1	22-08-2002
			ZA	9806362 A	22-01-1999